DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDAs 089903 and 089523

LABELING ORDER

West-Ward Pharmaceuticals Corp.
U.S. Agent for West-Ward Pharmaceuticals International Limited
2 Esterbrook Lane
Cherry Hill, NJ 08003

Attention: J. Barton Kalis
Sr. Director, Regulatory Affairs

Dear Mr. Kalis,

Please refer to your Abbreviated New Drug Applications (ANDAs) submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Prochlorperazine Edisylate Injection USP, 5 mg/mL.

On November 10, 2016, we sent you a letter invoking our authority under section 505(o)(4) of the FDCA to require safety related label changes to the labeling of antipsychotics, both conventional and atypical, to address the increased risk of falls that is likely due to well-known effects of these medications including, but not limited to, somnolence and orthostatic hypotension. The decision to require safety labeling changes was based on new safety information about this risk identified since these products were approved. You were directed to submit, within 30 days of the date of that letter, a supplement proposing changes to the approved labeling, or notify FDA that you do not believe a labeling change is warranted, and submit a statement detailing the reasons why such a change is not warranted.

Further reference is made to the electronic communication sent by the Carol Lee from the Office of Generic Drugs on December 27, 2016, to Mr. Kalis stating that you must submit a response to the November 10, 2016 Notification Letter, to which Mr. Kalis responded saying that process of finishing the updates are almost complete. You were also advised that requirements under section 505(o)(4) of the Act apply to NDAs, BLAs, and ANDAs without a currently marketed reference listed drug under an NDA, unless approval of your application has been withdrawn in the Federal Register. Therefore, even if you are not currently marketing your product, because your applications have not been withdrawn, you are required to comply with the safety labeling change requirements in section 505(o)(4) of the Act.

As of the date of this letter, the Agency has received no correspondence from you.

Under the authority of Section 505(o)(4)(E) of the FDCA, we are ordering you to make all of the changes in the labeling listed in the November 10, 2016, letter (attached).

Pursuant to Section 505(o)(4)(E), a changes being effected (CBE) supplement containing all of the changes to the labeling that are listed in the November 10, 2016, letter must be received by FDA by March 10, 2017, for Haloperidol Tablets, USP.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission:

SAFETY LABELING CHANGES UNDER 505(o)(4) – CHANGES BEING EFFECTED

Alternatively, by February 28, 2017, you may appeal this Order using the Agency's established formal dispute resolution process as described in 21 CFR 10.75 and the Guidance for Industry, "Formal Dispute Resolution: Appeals Above the Division Level." http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM343101.pdf. The appeal should be submitted as a correspondence to your ANDA referenced above. Identify the submission as "**Formal Dispute Resolution Request**" both on the cover letter and on the outside envelope. A copy of the submission should be sent to:

Khushboo Sharma
CDER Formal Dispute Resolution Project Manager
Food and Drug Administration
Office of New Drugs
White Oak Building 22, Room 6486
10903 New Hampshire Avenue
Silver Spring, MD 20993

In addition, to expedite coordination of any such appeal, a copy of the submission should also be sent to:

Carol Lee
Labeling Project Manager
Office of Generic Drugs
Food and Drug Administration
Bldg. 75, Room 3631
10903 New Hampshire Avenue
Silver Spring, MD 20993

Refer to the Guidance for Industry, "Formal Dispute Resolution: Appeals Above the Division Level" for further instruction regarding the content and format of your request. Questions regarding the formal dispute resolution process may be directed to Khushboo Sharma, CDER Formal Dispute Resolution Project Manager, at (301) 796-1270. Appeals received by the Agency later than February 28, 2017, will not be entertained.

Failure to respond to this Order within the specified timeframes is a violation of section 505(o)(4) of the FDCA and could subject you to civil monetary penalties under section 303(f)(4) of the FDCA, 21 U.S.C. 333(f)(4), in the amount of up to $250,000 per violation, with additional penalties if the violation continues uncorrected. Further, such a violation would cause your product to be misbranded under section 502(z) of the Act, 21 U.S.C. 352(z), which could subject

you to additional enforcement actions, included but not limited to seizure of your product and injunction.

If you have any questions, contact Carol Lee, Labeling Project Manager, at (240) 402-6244 or carol.lee@fda.hhs.gov.

Sincerely,

Kathleen Uhl, M.D.
Director, Office of Generic Drugs
Center for Drug Evaluation and Research

ENCLOSURE: Safety Labeling Change Notification Letter

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

ANDAs 089903
083329

SAFETY LABELING CHANGE NOTIFICATION

West-Ward Pharmaceuticals Corp
U.S. Agent for Eurohealth International Sàrl
2 Esterbrook Lane
Cherry Hill, NJ 08003

Attention: J. Barton Kalis
Director Regulatory Affairs

Dear Mr. Kalis:

Please refer to your Abbreviated New Drug Applications (ANDAs) submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Prochlorperazine Edisylate Injection USP, 5 mg/mL (ANDA 089903) and Chlorpromazine Hydrochloride Injection USP, 25 mg/mL (ANDA 083329).

Section 505(o)(4) of the FDCA authorizes FDA to require holders of approved new drug applications (NDAs) and biological license applications (BLAs) to make safety related labeling changes based upon "new safety information," as defined in section 505-1(b)(3) of the FDCA, about which FDA becomes aware after approval of the drug or biological product. Requirements under section 505(o)(4) apply to NDAs, BLAs, and ANDAs without a currently marketed reference listed drug approved under an NDA, including discontinued products, unless approval of an application has been withdrawn in the Federal Register. Therefore, the requirements described in this letter apply to you, unless approval of your application has been withdrawn in the Federal Register.

Since the referenced ANDAs were originally approved, we have become aware of an association between increased risk of falls and the use of antipsychotics, both conventional and atypical.

A summary of post-marketing evidence from the literature and the FDA Adverse Event Reporting System suggests a consistent association between antipsychotics and fall risk, especially in elderly populations. This increased risk of falls is likely due to well-known effects of these medications including, but not limited to, somnolence and orthostatic hypotension.

We consider this information to be "new safety information" as defined in section 505-1(b)(3) of the FDCA.

In accordance with section 505(o)(4) of the FDCA, we are notifying you that based on the new safety information described above we believe that the new safety information should

be included in the labeling for antipsychotic drugs, including the referenced ANDAs, as follows:

In Warnings, after Neuroleptic Malignant Syndrome, add the following subsection:

Falls
[INSERT DRUG PRODUCT] may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls and, consequently, fractures or other injuries. For patients with diseases, conditions, or medications that could exacerbate these effects, complete fall risk assessments when initiating antipsychotic treatment and recurrently for patients on long-term antipsychotic therapy.

In accordance with section 505(o)(4), within 30 days of the date of this letter, you must submit a supplement proposing changes to the approved labeling in accordance with the above direction, or notify FDA that you do not believe a labeling change is warranted, and submit a rebuttal statement detailing the reasons why such a change is not warranted. If you submit a supplement that includes only language identical to that specified above, the supplement may be submitted as a changes being effected (CBE-0) supplement. If the supplement includes proposed language that differs from that above, submit a prior approval supplement (PAS). Your supplement should only include proposed changes made in accordance with the above direction. Any other proposed labeling changes should be submitted in a separate supplement and should not be identified as a safety labeling change.

We have determined that an extension of the discussion period will be warranted to allow us to complete our review and reach agreement on the content of the labeling. Therefore, the discussion period for your supplement or rebuttal statement will begin when the submission is received, and will end within 150 days from the date of this letter, unless additional discussion extensions are warranted.

Failure to submit a response within 30 days may subject you to enforcement action, including civil money penalties under section 303(f)(4)(A), misbranding charges under section 502(z), and an order under 505(o)(4) to make whatever labeling changes FDA deems appropriate to address the new safety information.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate:

SAFETY LABELING CHANGES UNDER 505(o)(4) - PRIOR APPROVAL SUPPLEMENT

OR

SAFETY LABELING CHANGES UNDER 505(o)(4) – CHANGES BEING EFFECTED

OR

SAFETY LABELING CHANGES UNDER 505(o)(4) – REBUTTAL (CHANGE NOT WARRANTED)."

Prominently identify subsequent submissions related to the safety labeling changes supplement with the following wording in bold capital letters at the top of the first page of the submission:

SUPPLEMENT <<insert assigned #>>
SAFETY LABELING CHANGES UNDER 505(o)(4) - AMENDMENT

If you have any questions, contact Carol Lee, Labeling Project Manager, at (240) 402-6244 or carol.lee@fda.hhs.gov.

Sincerely,

{see appended signature page}

For Edward M. Sherwood
Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

CAROL A HOLQUIST
11/10/2016

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

ANDAs 074531
089523

SAFETY LABELING CHANGE NOTIFICATION

West-Ward Pharmaceuticals Corp.
U.S. Agent for West-Ward Pharmaceuticals International Limited
2 Esterbrook Lane
Cherry Hill, NJ 08003-4099

Attention: J. Barton Kalis
Sr. Director, Regulatory Affairs

Dear Mr. Kalis:

Please refer to your Abbreviated New Drug Applications (ANDAs) submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Fluphenazine Decanoate Injection USP, 25 mg/5 mL (ANDA 074531) and Prochlorperazine Edisylate Injection USP, 5 mg/mL (ANDA 089523).

Section 505(o)(4) of the FDCA authorizes FDA to require holders of approved new drug applications (NDAs) and biological license applications (BLAs) to make safety related labeling changes based upon "new safety information," as defined in section 505-1(b)(3) of the FDCA, about which FDA becomes aware after approval of the drug or biological product. Requirements under section 505(o)(4) apply to NDAs, BLAs, and ANDAs without a currently marketed reference listed drug approved under an NDA, including discontinued products, unless approval of an application has been withdrawn in the Federal Register. Therefore, the requirements described in this letter apply to you, unless approval of your application has been withdrawn in the Federal Register.

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A summary of post-marketing evidence from the literature and the FDA Adverse Event Reporting System suggests a consistent association between antipsychotics and fall risk, especially in elderly populations. This increased risk of falls is likely due to well-known effects of these medications including, but not limited to, somnolence and orthostatic hypotension.

We consider this information to be "new safety information" as defined in section 505-1(b)(3) of the FDCA.

In accordance with section 505(o)(4) of the FDCA, we are notifying you that based on the new safety information described above we believe that the new safety information should be included in the labeling for antipsychotic drugs, including the referenced ANDAs, as follows:

In Warnings, after Neuroleptic Malignant Syndrome, add the following subsection:

Falls
[INSERT DRUG PRODUCT] may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls and, consequently, fractures or other injuries. For patients with diseases, conditions, or medications that could exacerbate these effects, complete fall risk assessments when initiating antipsychotic treatment and recurrently for patients on long-term antipsychotic therapy.

In accordance with section 505(o)(4), within 30 days of the date of this letter, you must submit a supplement proposing changes to the approved labeling in accordance with the above direction, or notify FDA that you do not believe a labeling change is warranted, and submit a rebuttal statement detailing the reasons why such a change is not warranted. If you submit a supplement that includes only language identical to that specified above, the supplement may be submitted as a changes being effected (CBE-0) supplement. If the supplement includes proposed language that differs from that above, submit a prior approval supplement (PAS). Your supplement should only include proposed changes made in accordance with the above direction. Any other proposed labeling changes should be submitted in a separate supplement and should not be identified as a safety labeling change.

We have determined that an extension of the discussion period will be warranted to allow us to complete our review and reach agreement on the content of the labeling. Therefore, the discussion period for your supplement or rebuttal statement will begin when the submission is received, and will end within 150 days from the date of this letter, unless additional discussion extensions are warranted.

Failure to submit a response within 30 days may subject you to enforcement action, including civil money penalties under section 303(f)(4)(A), misbranding charges under section 502(z), and an order under 505(o)(4) to make whatever labeling changes FDA deems appropriate to address the new safety information.

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OR

SAFETY LABELING CHANGES UNDER 505(o)(4) – CHANGES BEING EFFECTED

OR

SAFETY LABELING CHANGES UNDER 505(o)(4) – REBUTTAL (CHANGE NOT WARRANTED)."

Prominently identify subsequent submissions related to the safety labeling changes supplement with the following wording in bold capital letters at the top of the first page of the submission:

SUPPLEMENT <<insert assigned #>>
SAFETY LABELING CHANGES UNDER 505(o)(4) - AMENDMENT

If you have any questions, contact Carol Lee, Labeling Project Manager, at (240) 402-6244 or carol.lee@fda.hhs.gov.

Sincerely,

{see appended signature page}

For Edward M. Sherwood
Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

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/s/

CAROL A HOLQUIST
11/10/2016

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/s/

CAROL N YUN
02/23/2017